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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/163,648	09/30/1998	SUSAN L. ACTON	MIA-025.02	5728

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INTELLECTUAL PROPERTY GROUP
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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/163,648	ACTON ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-16 and 44-60* is/are pending in the application.

4a) Of the above claim(s) *44 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-16 and 45-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed, 6-24-04 and 7-14-04 is acknowledged. The amendment amended claims 2, 8, 10, 15, 16, 45, 51, 53, 55, 57 and 59. Claims 2-16 and 45-59 are pending in this application.

Election/Restrictions

2. Applicant's election without traverse of Group II, claims 2-16, in the response dated 12-29-03 is acknowledged. Applicants cancelled claims 1, 17-43.

Applicants argue that for claims 44 and 60, the Examiner would not be burdened with additional search since claims are directed to antibodies which bind to the polypeptides of claims 2-16 and 45-59.

Applicants arguments have been considered but have not been found persuasive.

Applicants seem to imply that every reference that discloses the peptides of claims 2-16 and 45-59 would also disclose the antibodies that bind to these peptides. However, such an assumption is misplaced. Often times, the polypeptides are disclosed impendent of the antibodies. A search for the polypeptide and its antibody is not co-extensive. Thus a search would have to be extended for claims 44 and 60, where a reference that disclosed the peptides of Group II, did not disclose the antibodies. As such, the search would be burdensome and the restriction is appropriate.

This application contains claims 44 and 60 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

3. The submission of the references cited in the information disclosure statement filed 7-26-00 and 1-25-99 is acknowledged. An initialed copy of these information disclosure statement are attached with this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. The rejection of claims 10 and 53, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-16 and 45-59 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous office action and the reasons set forth below.

Applicants argue that the level of skill it the art is high and the disclosure of the application provides sufficient description relating to the generation of variant sequences. Further, the specification provides ample methods for assessing activities of the desired variants. Finally, the claims have been amended to recite "'at least one bioactivity of an ACE2 polypeptide,' thus reciting a combination of at least partial structural feature of a genus of polypeptides, as well as the biological activity."

Applicant's arguments filed 6-21-04 have been fully considered but they are not persuasive.

Applicants state that they have provided a combination of at least partial structural features as well as the biological activity. However, it is unclear what structural features Applicants have provide. The 90% homology of the SEQ ID NO: 2 is not static. Thus homologue can have variability from one to another. In essence, there is no core that each homologue must contain.

In University of Rochester v. Searle & Co., Case No. 03-1304 (Fed. Cir., Feb. 13, 2004), the Federal Circuit affirmed summary judgment of invalidity for failure to comply with the written description requirement because a compound recited in the claimed methods was defined purely by functional characteristics. In its decision, the court stated:

> "The patent also describes in detail how to make cells that express either COX-1 or COX-2, but not both, id. § 5.2, at cols. 8-20, as well as "assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product; and methods of treating diseases characterized by aberrant PGHS-2 activity using such compounds," id. at col. 8, ll. 2-7; see also id. § 5.6, at cols. 24-25. Such assay methods are in fact claimed in the '479 patent, i.e., Rochester's other patent based on the same disclosure. The '850 patent specification also describes what can be done with any compounds that may potentially be identified through those assays, including formulation into pharmaceuticals, routes of administration, estimation of effective dosage, and suitable dosage forms. Id. § 5.8, at cols. 27-34. As pointed out by the district court, however, the '850 patent does not disclose just "which

> 'peptides, polynucleotides, and small organic molecules' have the desired characteristic of selectively inhibiting PGHS-2." Univ. of Rochester, 249 F. Supp. 2d at 224. Without such disclosure, the claimed methods cannot be said to have been described.

Applicants disclosure is analogous in that the specification provides methods of making the 90% homologous peptides, assays for determining activity for ACE-2 bioactivity. However the specification fails to disclose just "'which 'peptides. . .'have the desired characteristic.'" For these reasons, the rejection is maintained.

6. Claims 2-16 and 45-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous office action and the reasons set for the below.

Applicants argue similar points made in the written description rejection. Applicants further assert that the "[t]he Examiner's rejection is apparently based on the numerous possibilities of various polypeptides comprising at least 90% identity to amino acid sequence of SEQ ID NO:2. . .Applicants submit, however, the number of possibilities of testing alone is not sufficient to maintain the present enablement rejection, as the tools to carry out such generation and/or identification of peptides, testing of bioactivities and identification of polypeptides having at least 90% identity. . . are in fact readily available to those of skill in the art in view of Applicant's disclosure and knowledge of those skilled in the art."

Applicant's arguments filed 6-21-04 have been fully considered but they are not persuasive.

The basis of the rejection was not merely the fact that one has to make numerous compounds and test each one individual. Rather the basis was the fact that the specification does not provide any guidance as to how to go about choosing the peptides having 90% homology. The specification lacks complete guidance to direct one of ordinary skill in the art as which amino acids to delete, add, or substitute in the peptides sequence obtain the 90% homologous analog. One has to arbitrarily and capriciously pick and choose the amino acids to be deleted, added, and substituted, then one has to test these peptides for the desired activity. The Webster's II dictionary defines undue as "exceeding the appropriate or normal: excessive." Certainly randomly picking and choosing amino acids deletions, substitutions, and or addition to obtain the desired peptide and then testing them for activity is certainly excessive and thus undue.

It is again emphasized that computer models are insufficient to provide guidance and give a prediction of activity. Although computers can be used to design drugs, "for the most part technicians must still screen many, many compounds to find their magic bullets." (see page 441). The article concludes that computer models are not an effective method of determining drug activity. "Even modest gains in the ability to predict drug activity from structural data will be enough to delight some computational biologist. 'Developing drugs is a vague science in which you synthesize a large number of compound." (See page 441). Moreover it is stated computers are unable at this point to design a drug from scratch (see page 441). These articles make these conclusions for any compound regardless of conservative or non-conservative substitutions. Indeed, peptide chemistry is replete with examples that demonstrate a single point mutation in a native sequence adversely affects activity. Here, Applicants the claims not only ask for single point mutations but numerous mutation throughout the amino acid sequence. None of these mutations have been demonstrate in the present application.

Rejection is maintained.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can normally be reached on (571) 272-0974. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta
Patent Examiner

BRUCE R. CAMPELL, PH.D
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